

APPENDIX B: ABNORMAL EVENTS INFORMATION

B.1 Potential Risk to Workers -- Laboratory-Acquired Infection

B.2 Potential Risk to Non-Workers from Contact with Biosafety Laboratory Workers

B.3 Accidents

Information derived for the accident analysis comes from publicly available literature with much of the data coming from the U.S. Army due to its premier role in the United States biological defense program which has been in existence for decades. This program, the U.S. Army Biological Defense Research Program (BDRP), is a research, development, test and evaluation (RDT&E) program conducted by the U.S. Department of Defense (DoD), with the Department of the Army (DA) serving as the executive agent. This program is conducted in accordance with 32 CFR 627 and under that scope (32 CFR 627.3) applies to all elements of the Army to include its contractors and subcontractors who use, produce, store, handle, or ship etiologic agents in support of the BDRP regardless of the source of the agent(s). This regulation essentially codifies the guidance of the CDC in its BMBL document (CDC 1999). This DA program has management responsibility for (1) the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), which is the lead laboratory in medical defense against biological warfare threats; (2) the U.S. Army Chemical Research, Development, and Engineering Command (CRDEC), which manages and conducts research, development, and engineering activities to provide non-medical defense against biological warfare threats; and (3) the U.S. Army Dugway Proving Ground (DPG), which is a major range and test facility supporting all DoD components and housing the Baker Laboratory Complex.

B.1 Potential Risk to Workers -- Laboratory-Acquired Infection

The potential for acquiring an infectious disease while working in a microbiological laboratory is significantly less than the occupational – related risks for healthcare workers. Indeed, the risk is very small if the appropriate microbiological facilities and containment devices are available, correct procedures and techniques are used, and adequate protective barriers are in place. These cautionary measures are needed because the quantities of microorganisms necessary for an infectious dose can be as little as one organism (Sewell 1995). Below, the historical perspective shows that in the early 1900s laboratory-acquired infections were common and pervasive throughout medical care facilities and laboratories. However, control of infection in laboratories has achieved a high level of sophistication to the point where virtually no reports of infection occur in biosafety laboratories in the United States today.

Historical Perspective In the last half of the 20th century the observations of physicians Oliver Wendell Holmes and Ignaz Semmelweis showed there was a connection between healthcare workers not washing their hands and patients acquiring certain diseases (Noskin and Peterson 2001). This started the concept of infection control which has subsequently driven equipment and facility design as well as the development of standardized procedures (CDC 1999; Collins and Kennedy 1999; Fleming et al. 1995; and Sewell 1995).

Since the early 1900s, various individuals conducted surveys or reported the connection between healthcare and laboratory workers contracting infectious diseases (CDC 1999; Collins 2000; Collins and Kennedy 1999; Pike 1979, 1976; Pike et al. 1965; Sewell 1995; and Sulkin and Pike 1951, 1949). The data they present are essentially published anecdotal reports, selected outbreaks with a specific microorganism, retrospective questionnaire-based surveys, and information presented at meetings related to laboratory-acquired infections and biosafety (Sewell 1995). These reports did result in the recognition that at least one primary route of transmission was aerosol, which in turn led to the development of the BSC. The consequence of using BSCs in laboratories was the later shift in focus from bacteria and rickettsia to viruses as the chief laboratory-associated infections. This is because the BSCs significantly reduced aerosol-induced infections to laboratory workers which were largely bacteria and rickettsia while the viruses are bloodborne and transmitted through contact (Sewell 1995).

During 1949 to 1974, the results of 3,921 infection reports were published in Health Laboratory Science journal (Pike 1976). As expected, bacterial infections were predominant with 1,669 cases (42.5 percent), followed by viral with 1,049 (26.7 percent), rickettsial with 573 (14.6 percent), fungal with 353 (9 percent), chlamydial with 128 (3.3 percent), parasitic with 115 (2.9 percent), and unspecified cases with 34 reports (0.9 percent). The bacterial infections were caused by various *Brucella* species, *Salmonella typhi*, *Francisella tularensis*, and *Mycobacterium tuberculosis*. Also, 90 viral infections were described with 36 percent caused by the hepatitis virus and Venezuelan equine encephalitis (VEE) virus. The rickettsial infections were due largely to *Coxiella burnetii* (Q fever) and the fungal infections were mostly due to *Histoplasma capsulatum* and *Coccidioides immitis*. It was noted in these reports that after 1955, the total number and frequency of bacterial, chlamydial, and rickettsial infections declined dramatically (Pike 1976).

Since the 1970s, when CDC issued their *Classification of Etiologic Agents on the Basis of Hazard*, (CDC 1974), which was essentially equivalent to the *NIH Guidelines for Research Involving Recombinant DNA* (NIH 2001), there has been both a reduction in surveys and analysis while reports of laboratory-acquired infection dropped in the United States. The BSLs and procedures established by the HHS, Public Health Service, CDC, and NIH in their BMBL document (now in its fourth edition [CDC 1999]) have been commonly accepted by most laboratories since the 1980s and are required to be implemented by those handling select agents covered under 42 CFR 72. The knowledge, the techniques, and the equipment to prevent most laboratory infections are available (Pike 1979). There is some indication that this is true when one reviews the admittedly anecdotal literature from more recent periods. “Some laboratory-acquired infections are now history (Collins and Kennedy 1999). For example, since 1991...no new reports have been found of tularaemia, plague, leptospirosis, cholera and typhoid fever, nor of the many rarer viral infections.” A recent bibliographic database (Collins 2000) starting with reports at the turn of the century and covering up through August 7, 2000, reveals substantial reductions of laboratory-acquired infections reported in the 1990s. There is a particularly notable lack of reported cases in the literature relating to laboratory-acquired infections in the United States during the last ten years.

The experience of the U.S. Army at their BDRP facilities over several decades provides further insight to the potential for laboratory-acquired infection. The DA program underwent a programmatic NEPA evaluation in 1989, the *Final Programmatic Environmental Impact Statement Biological Defense Research Program* (PEIS) (DA 1989). Since 1976, there have been no occurrences of overt disease in laboratory workers handling infectious organisms within the DA BSL-3 facilities, although in 1980, one focal infection with *F. tularensis* occurred at the site of a puncture wound (DA 1989).” There were also no deaths since 1964 (DA 1989). The PEIS (DA 1989) also estimated laboratory-acquired infection rates for its USAMRIID facility for different biocontainment levels (roughly equivalent to the CDC BSL levels) over different periods of time. For their BSL-3 equivalent laboratory operations from 1960 to 1962 they estimated there were six laboratory-acquired infections for a rate of 2 per million man-hours worked. For its BSL-4 equivalent laboratory operations from 1960 to 1969, DA estimated seven laboratory-acquired infections for a rate of 1 per million man-hours worked. These infections included subclinical infections and mild illnesses where hospitalization was not required (DA 1989).

Overall, the PEIS estimated the rate of public infection from USAMRIID as less than 0.001 per 1,000,000 person-years and the risk of death to a laboratory worker (for the “Defensive Research Period” 1970 to 1989) as 0.005 per 1,000,000 person-years (DA 1989). For the “Offensive or Weapons Period” (1954 to 1964) the values were about 5 orders of magnitude higher.

Routes of Exposure. The recognized routes of exposure for laboratory workers to contract infectious diseases is ingestion, inoculation, contamination of skin and mucous membranes, and inhalation (Sewell 1995). Today, many of these routes have limited potential because of facility design, equipment, and procedures. For example, some of the ingestion pathways are from mouth pipetting, contamination of articles or fingers placed in mouth, and consumption of food in the workplace. Due to the common acceptance of standard microbiological practices (CDC 1999) none of these should occur now. The primary routes of exposure remain inoculation

which occurs largely from the accidental needlestick, and inhalation from the numerous laboratory procedures which generate aerosols (Sewell 1995). Procedures which produce aerosols include, spontaneous discharge from a microbiological loop, the streaking of media, preparing microscopic slides, cooling a loop in culture media, and heating a loop in an open flame. Other devices often found in microbiological laboratories that can produce aerosols are centrifuges, blenders, homogenizers, shakers, sonicators, and mixers.

Small-Animal Handling. Small animals (rodents) used in research and development laboratories may host a variety of bacterial, viral, fungal and parasitic pathogens. However, it is possible to be virtually free of these pathogens if the laboratory adheres strictly to standard operating procedures (SOPs), maintains a high standard of quality for anything that enters the rodent facility (feed, bedding materials, and the animals themselves), utilizes rodent housing that allows for high standards of cleanliness for caging and ventilation, and overall containment design of the rodent facility.

One of the main risks to animal handlers and researchers comes from rodent allergens. Workers who are in regular contact with the rodents may develop sensitivities to them. Multiple independent studies have shown that about 21 percent of laboratory animal workers have laboratory animal allergy (LAA) (Fleming and Hunt, 2000). This may result in significant morbidity leading to reduced productivity and health care requirements. Immune responses to the allergens cause mucous production, swelling, and inflammation. The most common symptom is allergic rhinoconjunctivitis which results in nasal congestion, clear nasal discharge, sneezing, and itchy watery eyes. Skin reactions occur in about 40 percent of affected workers. These manifest as contact urticaria hives or eczema, a chronic itchy rash (Fleming and Hunt, 2000). Another immunologic respiratory disease which is less common is hypersensitivity pneumonitis resulting in acute flu-like symptoms to coughing and shortness of breath to an insidious wasting illness (Bascom 1996).

For mice (*Mus musculus*) there are three allergens: Mus m 1 (prealbumin) [hair, dander, and urine], Mus m 2 [hair and dander], and albumin [urine]. For rats (*Rattus norvegicus*) there are two allergens: Rat n 1A (pre-albumin) and Rat n 1 B (euglobulin) [hair, dander, urine, serum or saliva]. Highest exposures are to cage changers, room cleaners, and animal feeders. Allergen concentrations are higher with increased animal density and decreased relative humidity.

Workers with preexisting allergies or asthma are at increased risk of developing LAA (Fleming and Hunt, 2000). As expected animal handlers and caretakers develop allergic symptoms more frequently than those who do not work in direct contact, or put another way increased exposure correlates with increased symptom development. Animal cage technicians receive the highest exposure to allergens. For example, rat caretaking results in: cage cleaning mean allergen levels of 21 ng/m³ (for rats) and maximum of 310 ng/m³; handling 12 ng/m³; surgery and sacrifice 3 ng/m³ (Bascom 1996). Workers with the specific antibody to the allergen animal protein are 100 percent likely to continue to have allergic disease, and 10 percent would develop occupational asthma (Bascom 1996). Increasing the number of air-exchanges reduces the amount of allergen in the air and hence the worker exposure.

Aside from exposure to allergens, workers may also be exposed to zoonotic diseases. Research animal facilities have experience with *Brucella spp.*, *Francisella tularensis*, *Mycobacterium tuberculosis*, *Salmonella spp.*, *Shigella spp.*, *Coxiella burnetii*, and hepatitis A virus, to name a few. Transmission of zoonotic disease in research animals that are naturally infected is rare with the exception of Q-fever and lymphocytic choriomeningitis. Pathogens transmitted by mice have included *Microsporum* and *Trichophyton*, *Leptospira interrogans*, *Salmonella spp.*, *Shigella spp.*, and lymphocytic choriomeningitis (an arenavirus) (Bascom 1996).

Risk Associated with Biotoxin Research. There are three possible routes of exposure to these toxins which are inhalation, dermal absorption, and ingestion. Inhalation of bacterial exotoxins in the laboratory environment is very rare, and most are not readily absorbed through the skin (Fleming and Hunt, 2000). The highest likelihood of exposure is through the inadvertent needlestick (discussed earlier in this appendix). There is only one report of botulism associated with the handling of the agent or toxin in the laboratory and this occurred prior to 1950 (Fleming and Hunt, 2000).

Appendix I of the BMBL contains guidelines for work with toxins of biological origin. Work with most toxins can be performed safely in BSL-2 facilities using appropriate containment procedures and equipment unless the physical state of the toxin (e.g., a powder) or the volume requires handling in a BSL-3 laboratory (Fleming and Hunt, 2000). Volatility is not a concern with most toxins although it is recommended that open handling be done in a properly ventilated BSC to contain aerosols inadvertently produced. Inactivation of these toxins on surfaces can be easily accomplished with a 0.1 to 0.5 percent sodium hypochlorite solution, although sodium hydroxide and formalin are also effective. Temperatures in excess of 120°C for a minimum of 20 minutes are also effective at inactivation of most proteinaceous bacterial toxins meaning that autoclaving would inactivate them. Fleming and Hunt (2000) provide guidance on working safely with biological toxins, their storage, personal protective equipment requirements, and means of inactivation.

Transfer of some toxins are exempt under the “select agent” rule (42 CFR 72.6). Those exempt are those used for biomedical research at an LD₅₀ for vertebrates of no more than 100-ng/kg body weight. National standard toxins used for biological potency testing as described in 9 CFR 113 are also exempt.

B.2 Potential Risk to Non-Workers from Contact with Biosafety Laboratory Workers

One concern that members of the public may have is the potential for the proposed biosafety laboratory workers to inadvertently transmit diseases to other workers, family members, or the general public. Infectious agents may be transmitted through a variety of direct (communicable from one host to another) and indirect contact with an infected individual. It is by understanding the infectious cycle of the respective microorganism that is possible to identify the potential for transmission and means of mitigation. Some organisms require a vector, such as a flea, tick, or rodent, to transmit the infectious agent from one person to another. Other infectious microorganisms are directly contagious from one person to another. “Organisms that survive primarily or entirely in the human host and are spread through sexual contact, droplet nuclei, and close physical contact can be readily carried to any part of the world. For example, Acquired Immune Deficiency Syndrome (AIDS), tuberculosis, measles, pertussis, diphtheria, and hepatitis B are easily spread...Organisms that have animal hosts, environmental limitations, arthropod vectors, or complicated life cycles become successively more difficult to “transplant”...Epidemics of dengue fever and yellow fever cannot appear in a geographic area unless competent mosquito vectors are present. Schistosomiasis cannot spread in an environment unless a suitable snail intermediate host exists in that region” (Wilson 1995).

The tools to deal with transmission issues are vaccines and drugs, and vector-control methods such as pesticides. Of course, the primary means of defense is to limit all contact with infectious organisms and insure that they are destroyed or inactivated when they are on environmental surface or disposed in waste while still in the laboratory.

Historical Perspective. The literature is confusing with regard to the transmission of infectious agents between laboratory workers and the outside. Unfortunately, some of these infections have been transmitted from those workers to members of their families and to others outside the laboratory (Collins and Kennedy 1999). No specific statistical information was readily available on this subject. The only information specific to this is found in the information from the DA and the CDC.

According to the U.S. Army PEIS for the BDRP, there have never been any occurrences of infections in non-laboratory workers or in the general community arising from organisms handled in its BSL-3- or BSL-4-equivalent facilities associated with the BDRP (DA 1989). Similarly, discussion with the CDC in Atlanta about its BSL-3 and BSL-4 laboratories revealed that they have never had a documented case of a laboratory worker’s family members or other members of the public acquiring a disease associated with its laboratory operations (PC 2001a).

B.3 Accidents

Accidents associated with microbiological laboratories are generally thought of in terms of what might be considered routine accidents that have a reasonable probability of occurrence, but a very low consequence. These accidents would be leaking specimen/sample containers, spills involving broken glass or other containers, spillage and breakage in BSCs and centrifuge accidents (Collins and Kennedy 1999). Many of the laboratory-acquired infections may have resulted from these types of routine minor accidents. A literature search and discussions with laboratory regulators (such as the CDC, NIH, and the U.S. Army) revealed no examples of infectious materials released due to catastrophic accidents involving microbiological laboratories. In referring to these events the Army states that “The likelihood of such catastrophic occurrences is too small to be considered as reasonably foreseeable. No such event has occurred in the more than 50 years in which the military has been conducting biological defense activities (DA 1989).”

Historical Perspective. Researchers and preparers of infection incident summaries compiled information on accidents related to laboratory operations and specifically laboratory-acquired infections relating to accidents. In the review of 3,921 laboratory infections reported, 59 percent occurred in research laboratories (Pike 1976). About 70 percent of these resulted from working directly with infectious agents, some involving infectious aerosols (13 percent), and some from accidents (18 percent) (Sewell 1995). Overall, accidents were the second greatest source (initiator) of infections. Seventy percent of them were due to accidental inoculation (over 40 percent) with the remaining due to splashes and spills (about 30 percent). Another potential aerosol-producing accident, centrifuge accidents, results in relatively few laboratory-acquired infections, but a single incident often exposes several individuals (Sewell 1995).

The U.S. Army’s extensive experience (DA 1989) can be helpful in evaluating the potential for accidents involving infectious agents. The PEIS states “there have been laboratory accidents that resulted in potential exposures; however, prior immunization or immediate treatment with the appropriate therapy has averted the possible development of clinical disease... (DA 1989). The outstanding safety record (no illness resulting from laboratory exposure to agents or toxins in the last 10 years) at USAMRIID...and DPG...is indicative of how safely research with hazardous infectious organisms can be conducted. They additionally state that there have been no accidents or incidents among laboratory workers, their close associates, or the general community from the biological materials used specifically in the development of rapid diagnosis and detection systems (DA 1989). The Army further noted that during its many years of operations at Fort Detrick, they did not cause a single case of infection in the surrounding community (up through 1989). A more recent case of human glanders did occur there (CDC 2000c) but the individual recovered due to effective treatments.

Accident Scenarios from other NEPA Documents. Various NEPA accident scenarios have been postulated for infectious agents in BSL-3 laboratories (BMI 1993; DA 1989, 1992, 1996). Three of these NEPA documents present accident analyses which are termed as maximum credible events (MCE). The analysis of MCEs are required under the U.S. Army regulations (32 CFR 627). The documents described the MCEs as realistic events that have some probability of occurrence and resulting in maximum potential consequences. Two of these documents are EAs

for relatively small operations (BMI 1993 and DA 1996). The other two are EISs, one for a military installation (DA 1992) and the other a PEIS for the entire U.S. Army BDRP (DA 1989). Each accident approach is described briefly, except for the PEIS accident which is described in more detail.

The first, scenario for a BSL-3 facility in Ohio (BMI 1993), involved an accident that resulted in a release of exotoxin from the common soil pathogen, *Clostridium botulinum*. Three different toxins were planned for use in the facility (botulinum, ricin, and *Staphylococcal* enterotoxin B), but botulinum toxin was chosen because it was determined to be the most toxic of the three. The scenario involved the release of an aerosol equivalent in amount to one of their standard tests in the interior of a Class III BSC followed by release through the cabinet filtration system. The BSC exhausts through two HEPA filters in series with each removing 99.97 percent of the aerosol. The EA analysis also considered an accident relating to microorganism handling in which the organisms were not contained within a BSC as not being a credible accident since the only open culture handling, including packaging and un-packaging, is done inside their BSCs. They similarly discounted fire, explosion, loss of ventilation control, airplane crash, earthquake, and flooding as also not being credible events to initiate accidents. They determined that there was no effect on humans due to the release which was several orders of magnitude lower than the no-effect dose (BMI 1993).

The second EA involves the Armed Forces Institute of Pathology (AFIP) at Fort Detrick in Frederick, MD (DA 1996). This facility handles primarily *Brucella spp.* bacteria, which are normally transmitted by direct contact with the secretions of body fluids, aborted fetuses of infected animals, and by ingesting contaminated meat. *Brucella* is virulent (readily able to cause disease) and the infective dose can result from less than 10 microorganisms (DA 1996). While not explicitly stated, an accident analysis was not performed for the EA since the anecdotal information suggests there should be no reasonable probability of an accident event. Only one presumptive case of Brucellosis infection is identified in a worker (blood test suggested exposure but culturing could not prove the presence of the organism) but did not result in development of the disease. No incidence of secondary transmission of disease to those outside of the AFIP laboratory has been reported (DA 1996).

The third NEPA document is the EIS for the Life Sciences Test Facility at the Dugway Proving Grounds (DA 1992). This document reviewed accident scenarios and identified those considered by the DA to be reasonably foreseeable. The review covered two intentional release scenarios, ten accidental release scenarios, and six unexpected external event scenarios. The only scenario determined to be reasonably foreseeable was laboratory-acquired infection. This facility is also part of the Army's BDRP and is also discussed in the PEIS.

In the fourth NEPA document the DA considered an MCE analogous to a "worst case analysis" in Appendix A9 of the PEIS (DA 1989). However, the PEIS states:

"It has been determined that releases of aerosols of biological materials from facilities performing BDRP studies under appropriate containment conditions are not reasonably foreseeable. Catastrophic events, such as an airplane crash directly on a facility, have been perceived as a potential cause of aerosol release; however, it has been determined that the

probabilities of such events are too small to be considered reasonably foreseeable and/or the quantity of organisms on hand are too low to be of any risk from such an event...For the purpose of perspective and information, this appendix also presents estimates of the extent of potential impacts, under various conditions, resulting from the accidental releases of biological aerosols from the primary BDRP facilities. The findings are presented even though the event or series of events are not considered to be reasonably foreseeable. These estimates support the determination that such events would be noncatastrophic. Since the estimates show impact would occur only within the primary site boundaries...or within a few meters for other sites, they are not of catastrophic dimensions. The estimates also respond to the reasonable public interest in what might happen if the unforeseeable does occur and in whether the public would be at risk. The conclusion reached is that they are not.”

The MCE bioagent accident from the PEIS (DA 1989), Appendix A9 is presented as follows:

Initial conditions:

- A typical BSL-3 equivalent laboratory exists at USAMRIID and is designed to exceed CDC guidelines.
- A centrifuge, the key piece of equipment in this scenario, is in a room and not in a BSC.
- The size of the room is 1,080 ft³ (30,240 liters), but since the room is under negative pressure and air flow is continuous, the volume of the duct from the room leading to the filter is also included (608 ft³ or 17,024 liters) for a total volume of 1,688 ft³ (47, 264 liters).
- The BSL-3 equivalent laboratory centrifuge room exhausts air via two filters in series, which are conservatively estimated to have 95 percent particulate removal efficiency, and air then exits through a roof stack.
- The only microorganism handled in the laboratory is a Rickettsial organism, *Coxiella burnetii*, which causes Q-fever, this organism is hardy and withstands laboratory manipulation with little or no loss in viability, is highly stable in aerosols and dies at a rate of about one percent per minute over a wide range of humidities (30 to 85 percent relative humidity) and temperature (0 to 30 °C). It is extremely infectious in a small particle aerosol.
- A single worker is working with one liter of *Coxiella burnetii* slurry.
- The worker places 165 milliliters of slurry into each of six 250-milliliter polypropylene centrifuge tubes AND fails to insert O-rings or tighten the centrifuge caps which are screw-on.

Accident scenario:

The centrifuge is turned on at 10,000 revolutions per minute for 30 minutes

- All six tubes leak;
 - *Some slurry leaks into the rotor.*
 - *Some slurry leaks into centrifuge compartment.*

- *Most of the slurry remains in the tubes.*
- *Most of the slurry that leaked into covered rotor is not aerosolized (99 percent).*
- *Only a fraction of the slurry that leaked into the centrifuge cabinet is aerosolized and 90 percent of that settles as droplets inside the chamber.*
- A few minutes after the centrifuge stops, the worker opens the centrifuge and reaches in to remove the rotor;
 - *He notices leak.*
 - *He gets assistance of two co-workers to help him manage the spill.*
 - *Four more workers enter the laboratory not knowing of the accident.*
 - *All seven workers may have been exposed to a dose of organisms sufficient to cause infection in unimmunized individuals.*
- The slurry is thixotropic (much like egg white) but due to centrifuging has a reduced viscosity (20 to 25 centipoise) containing about 20 percent dry solids.
- The percent aerosol recovery (aerosol efficiency is defined as the number of infectious doses of *Coxiella burnetii* rendered airborne in a one- to five-micron particle size) representing the maximum infectivity for man is determined to conservatively be 0.1 percent.

Result to the Workers:

- The accident immediately produces 9.9×10^9 airborne human infective doses at a 50 percent rate for contracting the disease (HID_{50}) contained in a 3x3x3-foot area above and around the centrifuge (756 liters).
- There are 1.3×10^3 HID_{50} per liter of air in the seconds after the lid was opened.
- The centrifuge operator, excited by the accident, was breathing 15 liters of air per minute and was in the confined aerosol for no more than 5 minutes and could have inhaled about 100,000 HID_{50} .
- The two co-workers coming to the operator's assistance were exposed to only a slightly less dose than the centrifuge operator.
- The other four workers were exposed for less than 1 minute to the aerosol after it was dispersed in the room and are unlikely to have been exposed to more than 100 to 300 HID_{50} .

Result to the General Population and Surrounding Environment:

The result to the general public was evaluated using a simple Gaussian plume-dispersion air model. In this type of model the downwind distance that a given concentration of microorganisms would travel is a direct function of the emission rate and an inverse function of the lateral and vertical dispersion and wind speed. Higher rates of emission result in greater downwind distances for a given concentration. Similarly, lower lateral dispersion, vertical dispersion, or wind speed result in greater downwind concentrations. Downwind concentration

is decreased as a consequence of environmental degradation (e.g., from oxygen and ultraviolet light). Modeling assumptions used were:

- The maximum number of aerosolized infectious doses presented to the filters is 9.9×10^5 HID_{50} .
- After passing the 95% efficient filters the accident releases 5×10^4 infectious doses.
- The release is a daytime event since that is when the work is done.
- The breathing rate is 15 L/min.
- The lung retention of respirable particles is determined to be one-half or less of the intake.
- A Pasquill stability class D is used which “is the most stable one which can occur during the day.”
- The mixing layer depth is 100 m for stable conditions.
- Lateral and vertical dispersion coefficients used are 9.02 m and 6.5 m, respectively. (Chosen for open level-terrain which is more conservative)
- The wind speed is 4.5 mph.
- The quantity of human infective doses, by simple Gaussian plume dispersion models, is expected to be dissipated to:
 - Less than 1 HID_{50} in 1 liter (L) of air at a distance of less than 2 m from the stack,
 - Less than 0.1 HID_{50} in 1 L of air at a distance of 16 m from the stack, and
 - Less than 0.01 HID_{50} in 1 L of air at a distance of 38 m from the stack.

Of the rickettsial agents, *Coxiella burnetii* probably represents the greatest risk of laboratory infection, according to the CDC. The organism is highly infectious and remarkably resistant to drying and environmental conditions. The infectious dose of virulent Phase I organisms in laboratory animals has been calculated to be as small as a single organism. The estimated HID (25-50) (inhalation) for Q fever is 10 organisms...Q fever is the second most commonly reported laboratory associated-infection (CDC 1999). The CDC and the WHO identify Q fever as a disease most commonly contracted occupationally by those working with livestock handling and processing, and those in laboratory and veterinary practice (CDC 2001b; WHO 1999).

Men who were previously vaccinated and then exposed to aerosols of 150 or 150,000 infectious doses of virulent *Coxiella burnetii* did not consistently become ill (Benenson 1959). Therefore, since the centrifuge operator would have been vaccinated as a requirement of employment, it is questionable whether he would contract the illness. Antibiotic treatment (doxycycline), soon after exposure, significantly decreases the chances of developing symptoms of the disease (Benenson 1959).

The DA conclusion for its MCE showed that the only worker to conceivably contract the illness as a consequence of the accident would be the centrifuge worker, and even that individual would likely not become ill.